IN BRIEF

AUTOIMMUNITY

Danger-free autoimmune disease in Aire-deficient mice.

Gray, D. H. D. *et al. Proc. Natl Acad. Sci. USA* **104**, 18193–18198 (2007)

Autoimmune regulator (AIRE) deficiency in mice results in the development of spontaneous, multiorgan autoimmunity, owing to a defect in the removal of autoreactive T cells. It has been proposed that stimulation of the innate immune system by environmental factors is required to activate these autoreactive T cells in the periphery (the danger theory of immune tolerance). Here, Gray *et al.* show that various compounds that are known to stimulate the innate immune system did not modulate the disease symptoms in *Aire*$^{-/-}$ mice on either the C57BL/6 or NOD (non-obese diabetic) background. A defect in Toll-like receptor signalling did not prevent the induction of autoimmunity in *Aire*$^{-/-}$ NOD mice. Furthermore, by using germ-free mice the authors showed that autoimmunity develops in the absence of microbial colonization in *Aire*$^{-/-}$ NOD mice. So, this study indicates that autoimmune disease in AIRE-deficient mice can develop without environmental stimulation.

ANTIGEN PRESENTATION

Portable flanking sequences modulate CTL epitope processing.

Le Gall, S., Stamegna, P. & Walker, B. D. *J. Clin. Invest.* **117**, 3563–3575 (2007)

Why is it that T-cell responses are often focused on just a single epitope? Might it be because the particular immunodominant peptide is preferentially processed and presented? Here, Le Gall *et al.* provide evidence, in HIV-1 infection, that this is indeed the case. A comparison of two overlapping CD8$^+$ T-cell epitopes from HIV-1 Gag revealed that processing and presentation of the immunodominant Gag epitope was faster and more efficient than that of the subdominant epitope. Cytosolic processing assays confirmed that peptides encompassing the immunodominant epitope are preferentially generated, whereas subdominant epitopes are frequently destroyed. Residues that flank the immunodominant epitope were found to confer this processing advantage, as when placed adjacent to the subdominant epitope they could transform it into a dominant one. The use of such portable epitope processing determinants in vaccine vectors could provide a means of optimizing T-cell responses.

VACCINES

Adjuvanting a DNA vaccine with a TLR9 ligand plus Flt3 ligand results in enhanced cellular immunity against the simian immunodeficiency virus.

Kwissa, M. *et al. J. Exp. Med.* **204**, 2733–2746 (2007)

In this report, Kwissa *et al.* examined the efficacy of Toll-like receptor (TLR) ligands on augmenting the immunogenicity of a DNA prime–boost vaccine against simian immunodeficiency virus (SIV). They injected rhesus macaques with FMS-like tyrosine kinase 3 ligand (FLT3L) to expand dendritic cells, and primed them with a DNA vaccine encoding immunodeficiency virus antigens mixed with ligands for TLR9 or TLR7 and TLR8. The animals were then boosted with DNA and twice with recombinant modified vaccinia virus Ankara that expressed the same antigens. Activating dendritic cells with a TLR9 ligand during the initial immunization with a DNA vaccine resulted in an enhanced antigen-specific CD8$^+$ T-cell response and improved control of viral loads after challenge with SIV.